

CLAIMS

1. An isolated polypeptide comprising a sequence according to SEQ ID 2, or a functional variant thereof.
2. A fusion protein comprising a polypeptide according to claim 1.
3. An isolated nucleic acid, or a variant thereof encoding the polypeptide according to
5 claim 1.
4. The nucleic acid according to claim 3, wherein the nucleic acid is a single-stranded or double-stranded RNA.
5. The nucleic acid according to claim 3, wherein the nucleic acid comprises a nucleic acid according to SEQ ID 11.
- 10 6. A vector, comprising a nucleic acid selected from the group consisting of the nucleic acid according to claim 3, and a nucleic acid coding for a polypeptide according to the SEQ ID 1 to 9 or SEQ ID 47.
7. The vector according to claim 6, wherein the vector is selected from the group consisting of a knock-out gene construct, a plasmid, a shuttle vector, a phagemid, a cosmid, a
15 viral vector, and an expression vector.
8. A cell comprising the nucleic acid according to claim 3.
9. A cell comprising the vector according to claim 6.
10. The cell according to claim 9, wherein the cell is a transgenic embryonic non-human stem cell.
- 20 11. A transgenic non-human mammal comprising the nucleic acid according to claim 3.
12. An antibody or an antibody fragment thereof, wherein the antibody is directed against the polypeptide according to claim 1 or against the nucleic acid according to claim 3.
13. A nucleic acid which comprises a nucleic acid having a sequence complementary to
25 the nucleic acid according to claim 3 or a non-functional mutant variant of the nucleic acid according to claim 3.
14. The nucleic acid according to claim 13, wherein the nucleic acid having a complementary sequence is an antisense molecule or an RNA interference molecule.

15. A vector comprising the nucleic acid according to claim 13.
16. The vector according to claim 15, wherein the vector is selected from the group consisting of a plasmid, a shuttle vector, a phagemid, a cosmid, a viral vector, and an expression vector.
- 5 17. A cell comprising the nucleic acid according to claim 13.
18. A cell comprising the vector according to claim 15.
19. A diagnostic comprising at least one compound selected from the group consisting of the polypeptide according to claim 1, a polypeptide according to SEQ ID 1 to 9 or SEQ ID 47, a nucleic acid encoding one of the aforementioned polypeptides, a variant of one of
10 the aforementioned nucleic acids, and an antibody or an antibody fragment directed against one of the aforementioned polypeptides, combined or together with suitable additives or auxiliaries.
20. The diagnostic according to claim 19, wherein the nucleic acid is a probe.
21. The diagnostic according to claim 20, wherein the probe is a DNA probe.
- 15 22. A pharmaceutical composition comprising at least one component selected from the group consisting of the polypeptide according to claim 1, a polypeptide according to SEQ ID 1 to 9 or SEQ ID 47, a functional variant of one of the aforementioned polypeptides, a nucleic acid encoding one of the aforementioned polypeptides, a variant of one of the
20 the aforementioned nucleic acids, a nucleic acid which is a non-functional mutant variant of one of the aforementioned nucleic acids, a nucleic acid having a sequence complementary to one of the aforementioned nucleic acids, a vector comprising one of the aforementioned nucleic acids, a cell comprising one of the aforementioned nucleic acids, a cell comprising the aforementioned vector, an antibody or a fragment of the antibody directed against one of the aforementioned polypeptides, an antibody or a fragment of the antibody directed
25 against a functional variant of one of the aforementioned polypeptides, a vector comprising a nucleic acid coding for one of the aforementioned antibodies, a cell comprising the vector comprising a nucleic acid coding for one of the aforementioned antibodies, and a cell comprising the vector comprising a nucleic acid coding for one of the aforementioned antibody fragments, combined or together with suitable additives or auxiliaries.

23. The pharmaceutical composition according to claim 22, wherein the nucleic acid having a complementary sequence is an antisense molecule or an RNA interference molecule.

24. A method of diagnosis of a liver disorder or an epithelial cancer, wherein at least one compound selected from the group consisting of a polypeptide according to the sequence of SEQ ID 1 to SEQ ID 9 or SEQ ID 47, a functional variant of one of the aforementioned polypeptides, a nucleic acid encoding one of the aforementioned polypeptides, a variant of one of the aforementioned nucleic acids, a nucleic acid which is a non-functional mutant variant of one of the aforementioned nucleic acids, a nucleic acid having a sequence complementary to one of the aforementioned nucleic acids, an antibody or a fragment of the antibody directed against one of the aforementioned polypeptides, and an antibody or a fragment of the antibody directed against a functional variant of one of the aforementioned polypeptides, is identified in the sample of a patient and compared with at least one compound of a reference library or of a reference sample.

25. The method according to claim 24, wherein the liver disorder, is a disorder selected from the group consisting of cirrhosis, alcoholic liver disease, chronic hepatitis, Wilson's Disease, heamochromatosis, hepatocellular carcinoma, benign liver neoplasms, and focal nodular hyperplasia.

26. The method according to claim 24, wherein the epithelial cancer is an adenocarcinoma of an organ selected from the group consisting of the lung, the stomach, the kidney, the colon, the prostate, the skin, and the breast.

27. A method of treating a patient suffering from a liver disorder or an epithelial cancer, wherein at least one component selected from the group consisting of a polypeptide according to SEQ ID 1 to 9 or SEQ ID 47, a functional variant of one of the aforementioned polypeptides, a nucleic acid encoding one of the aforementioned polypeptides, a variant of one of the aforementioned nucleic acids, a nucleic acid which is a non-functional mutant variant of one of the aforementioned nucleic acids, a nucleic acid having a sequence complementary to one of the aforementioned nucleic acids, a vector comprising one of the aforementioned nucleic acids, a cell comprising one of the aforementioned nucleic acids, a cell comprising the aforementioned vector, an antibody or a fragment of the antibody directed against one of the aforementioned polypeptides, an antibody or a fragment of the antibody

directed against a functional variant of one of the aforementioned polypeptides, a vector comprising a nucleic acid coding for the antibody, a cell comprising the vector comprising a nucleic acid coding for the antibody, and a cell comprising the vector comprising a nucleic acid coding for the antibody fragment, combined or together with suitable additives or auxiliaries, is administered to the patient in need of a the treatment in a therapeutically effective amount.

28. The method of treating according to claim 27, wherein the nucleic acid having a complementary sequence is an antisense molecule or an RNA interference molecule.

29. The method of treating according to claim 28, wherein the RNA interference molecule is administered in the form of a double stranded RNA or a vector expressing the double stranded RNA.

30. The method according to claim 29, wherein the RNA interference molecule has a size range selected from the group consisting of from 15 to 30 nucleotides.

31. The method according to one of claims 27 to 30, wherein the liver disorder, is a disorder selected from the group consisting of cirrhosis, alcoholic liver disease, chronic hepatitis, Wilson's Disease, heamochromatosis, hepatocellular carcinoma, benign liver neoplasms, and focal nodular hyperplasia.

32. The method according to one of claims 27 to 30, wherein the epithelial cancer is an adenocarcinoma of an organ selected from the group consisting of the lung, the stomach, the kidney, the colon, the prostate, the skin, and the breast.

33. A method of stimulating an immune response in a patient suffering from a liver disorder or an epithelial cancer, to a polypeptide according to the sequence of SEQ ID 1 to SEQ ID 9 or SEQ ID 47, or a functional variant thereof, wherein at least one component selected from the group consisting of a polypeptide according to the sequence of SEQ ID 1 to SEQ ID 9 or SEQ ID. No. 47, a functional variant thereof, a nucleic acid encoding one of the aforementioned polypeptides, a variant of one of the aforementioned nucleic acids, a vector comprising one of the aforementioned nucleic acids, a cell comprising one of the aforementioned nucleic acids, and a cell comprising the aforementioned vector, is administered to the patient in need of such treatment in an amount effective to stimulate the immune response in the patient.

34. A method for identifying at least one nucleic acid according to SEQ ID 10 to SEQ ID 19, or a variant thereof differentially expressed in a sample isolated from a patient relative to a reference library or a reference sample comprising the following steps:

- 5 (a) detecting the expression of at least one nucleic acid according to SEQ ID 10 to SEQ ID 19, or a variant thereof in a sample isolated from a patient,
- (b) comparing the expression of said nucleic acid(s) detected in step (a) with the expression of the said nucleic acid(s) in a reference library or in a reference sample,
- 10 (c) identifying said nucleic acid(s) which is (are) differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample.

35. A method of diagnosing a liver disorder or an epithelial cancer comprising the following steps:

- 15 (a) detecting the expression of at least one nucleic acid according to SEQ ID 10 to SEQ ID 19, or a variant thereof in a sample isolated from a patient,
- (b) comparing the expression of said nucleic acid(s) detected in step (a) with the expression of said nucleic acid(s) in a reference library or in a reference sample,
- 20 (c) identifying said(s) nucleic acid which is (are) differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample, and
- (d) matching said nucleic acid(s) identified in step (c) said nucleic acid(s) differentially expressed in a pathologic reference sample or pathologic reference library,

25 wherein the matched nucleic acid(s) is (are) indicative of the patient suffering from a liver disorder or an epithelial cancer.

36. The method according to claim 35, wherein step (a) at least 2 nucleic acids are identified.

37. The method according to claim 35, wherein in step (a) the detection of said nucleic acid(s) is (are) by PCR based detection or by a hybridization assay.

38. The method according to one of claims 35 to 37, wherein in step (b) the expression of said nucleic acid(s) is compared by a method selected from the group consisting of
5 solid-phase based screening methods, hybridization, subtractive hybridization, differential display, and RNase protection assay.

39. The method according to one of claims 35 to 38, wherein the sample isolated from the patient is selected from the group consisting of liver tissue, a liver cell, tissue from another organ subject to cancerous transformation, a cell from this organ, blood, serum,
10 plasma, ascitic fluid, pleural effusion, cerebral spinal fluid, saliva, urine, semen, and feces.

40. The method according to one of claims 35 to 39, wherein the reference sample is isolated from a source selected from a non-diseased sample of the same patient and a non-diseased sample from another subject.

41. The method according to one of claims 35 to 40, wherein the reference sample is
15 selected from the group consisting of liver tissue, a liver cell, blood, serum, plasma, ascitic fluid, pleural effusion, cerebral spinal fluid, saliva, urine, semen, and feces.

42. The method according to one of claims 35 to 41, wherein the reference library is an expression library or a data base comprising clones or data on liver disorder-specific expression of said nucleic acid(s) of step (a).

20 43. The method according to one of claims 35 to 42, wherein the pathologic reference sample is isolated from a source selected from a diseased sample from another patient suffering from a liver disorder or epithelial cancer.

44. The method according to claim 35 to 43, wherein the pathologic reference library is a data base comprising data on differential expression of said nucleic acid(s) in step (a) in
25 samples isolated from another patient suffering from a liver disorder or epithelial cancer relative to control expression in a reference sample or reference library.

45. The method according to claim 35 to 44, wherein the liver disorder, is a disorder selected from the group consisting of hepatocellular carcinoma, benign liver neoplasms, and cirrhosis.

46. The method according to claim 35 to 44, wherein the epithelial cancer is an adenocarcinoma of an organ selected from the group consisting of the lung, the stomach, the kidney, the colon, the prostate, the skin and the breast.

47. A method for identifying at least one polypeptide according to SEQ ID 1 to SEQ ID 9 or SEQ ID 47, or a functional variant thereof differentially expressed in a sample isolated from a patient relative to a reference library or a reference sample comprising the following steps:

- (a) detecting the expression of at least one polypeptide according to SEQ ID 1 to SEQ ID 9 or SEQ ID 47, or a functional variant thereof in a sample isolated from a patient,
- (b) comparing the expression of said polypeptide(s) detected in step (a) with the expression of said polypeptide(s) in a reference library or in a reference sample,
- (c) identifying said polypeptide(s) which is (are) differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample.

48. A method of diagnosing a liver disorder or epithelial cancers comprising the following steps:

- (a) detecting the expression of at least one polypeptide according to SEQ ID 1 to SEQ ID 9 or SEQ ID. No. 47, or functional variants thereof in a sample isolated from a patient,
- (b) comparing the expression of said polypeptide(s) detected in step (a) with the expression of said polypeptide(s) in a reference library or in a reference sample,
- (c) identifying said polypeptide(s) which is (are) differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample, and
- (d) matching said polypeptide i(s) identified in step (c) with said polypeptide(s) differentially expressed in a pathologic reference sample or pathologic reference library,

wherein the matched polypeptide(s) are indicative of the patient suffering from a liver disorder, or an epithelial cancer.

49. The method according to claim 48, wherein at least 2 polypeptides are identified.

50. The method according to claim 48 or 49, wherein the polypeptides are detected by a
5 method selected from the group consisting of gel electrophoresis, chromatographic techniques, immunoblot analysis, immunohistochemistry, enzyme based immunoassay, surface plasmon resonance, HPLC, mass spectroscopy, immunohistochemistry, and enzyme based immunoassay.

51. The method according to one of claims 48 to 50, wherein the polypeptides are compared by a method selected from the group consisting of two dimensional gel electrophoresis,
10 chromatographic separation techniques, immunoblot analysis, surface plasmon resonance, immunohistochemistry, and enzyme based immunoassay.

52. The method according to one of claim 48 to 51, wherein the sample isolated from a patient is selected from the group consisting of liver tissue, a liver cell, tissue from another organ subject to cancerous transformation, a cell from this organ, blood, serum, plasma,
15 ascitic fluid, pleural effusion, cerebral spinal fluid, saliva, urine, semen, and feces.

53. The method according to one of claims 48 to 52, wherein the reference sample is isolated is from a source selected from a non-diseased sample of the same patient and a non-diseased sample from another subject.

54. The method according to one of claims 48 to 53 wherein the reference sample is selected from the group consisting of liver tissue, a liver cell, blood, serum, plasma, ascitic fluid, pleural effusion, cerebral spinal fluid, saliva, urine, semen, and feces.

55. The method according to one of claims 48 to 54, wherein the reference library is an expression library or a data base comprising clones or data on liver disorder-specific expression of said polypeptide(s) of step (a).
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56. The method according to claim 48 to 55, wherein the pathologic reference sample is isolated from a source selected from a diseased sample from another patient suffering from a liver disorder and epithelial cancer.

57. The method according to claim 48 to 56, wherein the pathologic reference library is
30 a data base comprising data on differential expression of said polypeptide(s) of step (a) in

samples isolated from another patient, suffering from a liver disorder or epithelial cancer relative to control expression in a reference sample or reference library.

58. The method according to claim 48 to 57, wherein the liver disorders is a disorder selected from the group consisting of hepatocellular carcinoma, benign liver neoplasms, and cirrhosis.

59. The method according to one of claims 48 to 57, wherein the epithelial cancer is an adenocarcinoma of an organ selected from the group consisting of the lung, the stomach, the kidney, the colon, the prostate, the skin, and the breast.

60. A method of preventing a patient from developing a liver disorder or an epithelial cancer, wherein at least one component selected from the group consisting of a polypeptide according to the sequence of SEQ ID 1 to SEQ ID 9 or SEQ ID 47, a functional variant thereof, a nucleic acid encoding one of the aforementioned polypeptides, a variant of one of the aforementioned nucleic acids, a nucleic acid having a sequence complementary to one of the aforementioned nucleic acids, a nucleic acid which is a non-functional mutant variant of one of the aforementioned nucleic acids, a vector comprising one of the aforementioned nucleic acids, or a variant thereof, a cell comprising one of the aforementioned nucleic acids, or a variant thereof, and a cell comprising the aforementioned vector, is administered to the patient in need of such preventive treatment in a therapeutically effective amount.

61. A method of identifying a pharmacologically active compound comprising the following steps:

- (a) providing at least one polypeptide according to the SEQ ID 1 to 9 or 47, or a functional variant thereof,
- (b) contacting said polypeptide(s) with suspected to be pharmacologically active compound(s),
- (c) assaying the interaction of said polypeptide(s) of step (a) with said compound(s) suspected to be pharmacologically active,
- (d) identifying said compound(s) suspected to be pharmacologically active which directly or indirectly interact with said polypeptide(s) of step (a).

62. The method according to claim 61, wherein said polypeptide(s) of step (a) is (are) attached to a column, said polypeptide(s) is (are) attached to an array, contained in an electrophoresis gel, attached to a membrane, or is (are) expressed by a cell.

63. The method according to claim 61 or 62, wherein the interaction is assayed enzyme
5 or fluorescence based cellular reporter methods

64. The method according to claim 61 or 62, wherein the interaction is assayed by surface plasmon resonance, HPL, or mass spectroscopy.

65. The method according to claim 61, wherein the direct or indirect functional interaction of step (d) is selected from the group consisting of induction of the expression of said
10 polypeptide(s) of step (a), inhibition of said polypeptide(s), activation of the function of said polypeptide(s), and inhibition of the function of said polypeptide(s).